

**Notice of Allowability**

Application No.

10/779,399

Applicant(s)

UCKUN, FATIH M.

Examiner

Nashaat T. Nashed, Ph. D.

Art Unit

1656

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to amendment filed December 1, 2006.
2. ☒ The allowed claim(s) is/are 25-34.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some\* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. ☒ Information Disclosure Statements (PTO/SB/08),  
Paper No./Mail Date 12/13/06
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_
7. ☒ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other \_\_\_\_\_

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Applicant's election without traverse of Group I, claims 1 and 2, in the reply filed on November 2, 2006 is acknowledged.

The application has been amended as requested in the communications filed November 2, 2006; November 21, 2006; and December 1, 2006. Accordingly, claims 1-24 have been canceled, and new claims 25-33 have been entered.

Newly presented claims directed to a method of using the crystal were not restricted from the crystal because the crystal was found novel.

Claims 25-33 have been entered and pending.

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Eric E. DeMaster on January 12, 2007.

The application has been amended as follows:

Claim 26. The crystal of claim ~~425~~, wherein analysis of a pattern of X-ray diffraction from the crystal produces a structure defined by the atomic coordinates listed in Table ~~44~~.

Claim 27 A method for identifying a compound that inhibits BTK activity comprising:

(a) ~~preparing a crystal of amino acid residues~~ solution comprising 12 mg/ml of a BTK kinase domain of SEQ ID NO:4, 20 mM Tris/HCl, 50 mM NaCl, 2 mM DTT, and pH 8.5;

(b) crystallizing the BTK kinase domain at 4 °C using a hanging drop method, wherein the drop comprises 2 microliters of [a] ~~the solution of (a) comprising 2 mg/ml of purified BTK kinase domain~~ and 1 microliter of reservoir solution and is equilibrated with 600 microliters of the reservoir solution, wherein the reservoir solution comprises 20% polyethylene glycol-~~1000~~, 100 mM Tris/HCl, and 1 mM DTT, the reservoir solution being buffered at a pH of about 8.0;

(c) determining a structure of the BTK kinase domain of SEQ ID NO:4 by X-ray diffraction methods, wherein said structure is defined by the atomic coordinates of Table 1; and

(d) using said determined structure to identify a compound ~~that complements the crystal's determined structure, thereby identifying a compound that inhibits BTK activity.~~

Claim 28 A method for identifying a compound that inhibits BTK activity comprising:

- (a) obtaining the crystal of claim ~~425~~;
- (b) determining by X-ray diffraction ~~method~~, atomic coordinates defining a structure of the BTK kinase domain of SEQ ID NO:4; and
- (c) using the structure defined by the atomic coordinates to identify a compound that interacts with the BTK kinase domain and thereby identifying a compound that inhibits BTK activity.

Claim 29 The method of claim ~~4728~~, further comprising:  
(d) assaying the identified compound for BTK kinase inhibition activity.

Claim 30 A method for preparing a crystal of a BTK kinase domain comprising:

- (a) preparing a ~~purified BTK kinase domain~~ in a solution of 20mM Tris/HCl, pH 8.5, 50 mM NaCl, and 2mM DTT, and purified 12 mg/ml of the kinase domain ~~having the amino acid sequence of SEQ ID NO: 4~~; and
- (b) crystallizing the purified BTK kinase domain at 4 °C using a hanging drop method, wherein the drop comprises 2 microliters of [a] solution ~~(a) comprising 2 mg/ml of purified BTK kinase domain~~ and 1 microliter of reservoir solution comprising 20% polyethylene glycol-1000, 100 mM Tris/HCl, 1 mM DTT, buffered to a pH of about 8.0; and wherein the drop is equilibrated with 600 microliters of the reservoir solution.

Claim 31 A crystal prepared by the process of claim ~~2030~~.

Claim 32 The method of claim ~~4728~~, wherein said structure is defined by coordinates of Table ~~44~~.

Claim 33 The crystal of claim ~~2031~~, wherein analysis of a pattern of X-ray diffraction from the crystal produces a structure defined by the atomic coordinates listed in Table ~~44~~.

Claim 34 (New) The method of claim 27, wherein said structure is defined by coordinates of Table ~~44~~.

Claims 25-34 are allowed.

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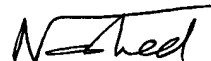
The following is an examiner's statement of reasons for allowance: The specification teaches the crystallization of the BTK kinase domain of SEQ ID NO: 4. Said domain crystallized in the orthorhombic space of  $P2_12_12_1$  having unit cell dimension of  $a = 45 \text{ \AA}$ ,  $b = 104 \text{ \AA}$ , and  $c = 116 \text{ \AA}$ . Also, the specification enabled and described methods of using the crystal to identify inhibitor for the BTK activity. The claims in instant application is directed to the specific crystal taught in the specification and method of making as well as a method of identifying inhibitors of the BTK activity. Since the crystal is not anticipated or obvious over the prior art of record, the claims are allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is 571-272-0934. The examiner can normally be reached on MTWTF.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Nashaat T. Nashed, Ph. D.  
Primary Examiner  
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